

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1-33. **(Canceled)**

34. **(Currently amended)** A method of reducing and conjugating a drug to an antibody ~~resulting in selectivity in the placement of the drug~~, comprising:

fully reducing the antibody with a reducing agent;

treating the fully reduced antibody with limiting amounts of a reoxidizing agent to reform at least one interchain disulfide bond of the antibody to form a partially reoxidized antibody, such that at least two interchain thiols remain; and

conjugating the drug to [[one]] an interchain thiol of the partially reoxidized antibody via a maleimide group.

35. **(Original)** The method of claim 34, wherein the reoxidizing agent is 5,5'-dithio-bis-2-nitrobenzoic acid, 4,4'-dithiodipyridine, 2,2'-dithiodipyridine, sodium tetrathionate or iodosobenzoic acid.

36. **(Previously Presented)** The method of claim 35, wherein the drug is a cytotoxic or cytostatic agent or an immunosuppressive agent.

37. **(Currently amended)** The method of claim 36, wherein the cytotoxic or cytostatic agent is a minor groove binder, an ester produced by reacting auristatin E with paraacetyl benzoic acid (AEB), an ester produced by reacting auristatin E with benzoylvaleric acid (AEVB), dovaline-valine-dolaisoleunine-dolaproline-phenylalanine (MMAF), monomethyl auristatin E (MMAE), or dimethylvaline-valine-dolaisoleunine-dolaproline-phenylalanine-p-phenylenediamine (AFP).

38. **(Currently amended)** The method of claim 34, wherein at least two drugs are conjugated to the partially reoxidized antibody and each drug is conjugated to [[one]] a distinct interchain thiol.

39. **(Original)** The method of claim 34, wherein the reducing agent is DTT or TCEP.

40-42. **(Cancelled)**

43. **(Previously Presented)** The method of claim 34, further comprising purifying the partially reoxidized antibody.

44-63. **(Cancelled)**

64. **(Currently amended)** A method of producing a conjugated antibody an antibody with selective conjugation of a drug comprising:

~~fully reducing the antibody for a period of time sufficient to produce interchain thiols, as determined by DTNB titration, by adding contacting an antibody solution with a large excess of a reducing agent and incubating the resulting solution at about 37 °C for about 30 minutes, to produce a fully reduced antibody;~~

~~purifying the fully reduced antibody;~~

~~partially reoxidizing the fully reduced antibody using an oxidizing agent to form at least one interchain disulfide bond by~~

~~cooling the fully reduced antibody to about 0 °C;~~

~~treating the fully reduced and cooled antibody with about 1.5 to about 2.5~~

~~molar equivalents of the oxidizing agent to form a reaction solution;~~

~~mixing the reaction solution by inversion;~~

~~allowing the reaction solution to incubate at about 0 °C for about 10 to 20~~

~~minutes and produce a partially reoxidized antibody;~~

~~purifying the partially reoxidized antibody;~~

~~conjugating [[the]] a drug to [[one]] an interchain thiol of the partially reoxidized antibody via a maleimide group to form [[a]] the conjugated antibody; and~~

purifying the conjugated antibody.

65. (Currently amended) The method of claim 64, wherein at least two drugs are conjugated to the antibody and each drug is conjugated to [[one]] an interchain thiol.

66-73. (Canceled)

74. (Currently amended) A method of preparing a mixture of antibody drug conjugates conjugate of a protein having one or more disulfide bonds and a drug, comprising:

fully reducing the protein antibodies with a reducing agent to form fully reduced antibodies;

partially reoxidizing the protein fully reduced antibodies with a reoxidizing agent to form partially reoxidized antibodies; and

conjugating [[the]] a drug reactive with free thiols to the protein to an interchain thiol of the partially reoxidized antibodies via a maleimide group to form antibody drug conjugates, wherein the average number of drugs per antibody in the mixture of antibody drug conjugates is less than the number of interchain thiols present on the fully reduced antibodies.

75-112. (Canceled)

113. (New) The method of claim 64, wherein the oxidizing agent is 5,5'-dithio-bis-2-nitrobenzoic acid, 4,4'-dithiodipyridine, 2,2'-dithiodipyridine, sodium tetrathionate or iodosobenzoic acid.

114. (New) The method of claim 64, wherein the drug is a cytotoxic or cytostatic agent or an immunosuppressive agent.

115. (New) The method of claim 114, wherein the cytotoxic or cytostatic agent is a minor groove binder, AEB, AEVB, MMAF, MMAE, or AFP.

116. (New) The method of claim 64, wherein at least two drugs are conjugated to the conjugated antibody and each drug is conjugated to an interchain thiol.

117. **(New)** The method of claim 64, wherein the reducing agent is DTT or TCEP.

118. **(New)** The method of claim 74, wherein the reoxidizing agent is 5,5'-dithio-bis-2-nitrobenzoic acid, 4,4'-dithiodipyridine, 2,2'-dithiodipyridine, sodium tetrathionate or iodosobenzoic acid.

119. **(New)** The method of claim 74, wherein the drug is a cytotoxic or cytostatic agent or an immunosuppressive agent.

120. **(New)** The method of claim 119, wherein the cytotoxic or cytostatic agent is a minor groove binder, AEB, AEVB, MMAF, MMAE, or AFP.

121. **(New)** The method of claim 74, further comprising purifying the plurality of partially reoxidized antibodies prior to conjugation with the drug.

122. **(New)** The method of claim 74, wherein the reducing agent is DTT or TCEP.

123. **(New)** The method of claim 74, wherein the mixture of antibody drug conjugates comprises antibodies conjugated to two drugs, antibodies conjugated to four drugs, and antibodies conjugated to six drugs.

124. **(New)** The method of claim 74, wherein the average number of drugs per antibody in the mixture of antibody drug conjugates is two.

125. **(New)** The method of claim 74, wherein the average number of drugs per antibody in the mixture of antibody drug conjugates is four.

126. **(New)** The method of claim 34, wherein the drug is MMAE and is conjugated to the partially reoxidized antibody via a maleimidocaproyl-valine-citrulline linker.

127. **(New)** The method of claim 64, wherein the drug is MMAE and is conjugated to the partially reoxidized antibody via a maleimidocaproyl-valine-citrulline linker.

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128. **(New)** The method of claim 74, wherein the drug is MMAE and is conjugated to the partially reoxidized antibodies via a maleimidocaproyl-valine-citrulline linker.